Derivation and comparative analysis of human pluripotent ESCs, iPSCs and SSCs: Convergence to an embryonic phenotype

Grant Award Details

Derivation and comparative analysis of human pluripotent ESCs, iPSCs and SSCs: Convergence to an embryonic phenotype

Grant Type: New Cell Lines

Grant Number: RL1-00670

Project Objective: The objective of this grant is to derive human pluripotent ESCs, iPSCs, and SSC and perform a comparative analysis.

Investigator:

Name:	Theo Palmer
Institution:	Stanford University
Type:	PI

Disease Focus: Fertility

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell, iPS Cell

Cell Line Generation: Adult Stem Cell, iPS Cell

Award Value: $1,409,243

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4 (NCE)

View Report

Grant Application Details

Application Title: Derivation and comparative analysis of human pluripotent ESCs, iPSCs and SSCs: Convergence to an embryonic phenotype

Public Abstract: This is an unprecedented time in stem cell biology and regenerative medicine. Today, we have cell lines and tools that did not exist just a few years ago. Indeed, human embryonic stem cells (hESCs) were derived from pre-implantation embryos just 10 years ago; more recently in the past year, cells with extensive similarities to ESCs have been derived via genetic reprogramming of ordinary fetal and adult skin cells in both mice and humans. These induced-pluripotent stem cells (IPSCs) have been shown to have many properties similar to hESCs. Also recently, and surprisingly in mice, a new source of cells that does not require genetic manipulation has been identified, namely mouse spermatogonial stem cells (mSSCs). These cells also demonstrate extensive similarity to mouse ESCs. However, human SSCs (hSSCs) have not yet been reported though our preliminary data presented here lends credence to their derivation. Our goal is to derive hIPSCs and hSSCs – two pluripotent cell types – from the same men and compare key characteristics to those of hESCs. We suspect human pluripotent cell types derived from these three different sources may differ in key characteristics including their ability to contribute to both the germ cell (egg and sperm) and somatic lineages (endoderm, mesoderm and ectoderm) and thus may provide an optimal or ideal resource for unique basic developmental genetic, pre-clinical and/or clinical applications. Specifically, our aims are to: 1) Derive additional hSSC and hIPSC lines. 2) Compare hSSCs, hESCs and IPSCs in terms of critical molecular, genetic and developmental characteristics. 3) Incorporate well-characterized first-generation hSSCs and IPSCs into a human pluripotent stem cell bank for broad distribution to the scientific community. Traditionally, development was considered to be a progression towards the irreversible reduction of potential to form diverse cell lineages (with the notable exception of germ cell development). However, in light of recent results, this view has been permanently altered. This proposal seeks to take advantage of unique resources and tools to derive novel cell lines, probe the breadth of potential of hIPSCs, hSSCs and hESCs and optimize use of appropriate pluripotent cell types for basic, pre-clinical and clinical applications. Note: It is necessary that we compare isogenic hIPSC and hSSC pairs with low-passage hESCs, grown under the same conditions; thus, this work must use “non-federal” hESCs and is not fundable by federal mechanisms.

Statement of Benefit to California:	Human embryonic stem cells are classically derived from human embryos that are not suitable for, or are in excess of, the reproductive needs of infertile men and women who present to assisted reproductive clinics. Evidence suggests that human embryonic stem cells can differentiate to many different cell types in the body and in fact, perhaps all the different cell types present in the adult. Thus, much excitement surrounds the possibility that the potential of human embryonic stem cells might be used to develop novel cell-based therapeutics to ease the tremendous burden of common, chronic disease and injury to the citizens of California. Many diseases and injuries, from birth, to childhood and adulthood, have a cellular basis and indeed may arise in the germ cells, the egg and sperm, or early embryo. A particular cell type, or process within a group of cells that form a tissue, may be specifically defective in disorders that range from diabetes to cardiac and neurodegenerative disorders as well as prevalent cancers. Nonetheless, the hope of novel cell-based therapies must be balanced by the realization that immunological rejection after transplantation will be an obvious hurdle unless we can make pluripotent cell lines that are compatible to individual genetic makeup. In this application, we propose to derive isogenic pairs of human pluripotent stem cells (human induced pluripotent stem cells and human spermatogonial stem cells) from the same men and characterize the potential of different cell types to contribute to both germ line and somatic lineages, relative to human embryonic stem cells. This research will benefit those in California by using our team's extensive experience and tools to produce high quality, well-characterized lines for banking and distribution widely throughout the scientific community. These cell lines constitute a genetic match for potential cell-based therapies, and also provide a system for the study of human genetic disorders and/or pharmacological properties. Moreover, given the controversial nature of human embryonic stem cells, this research provides a systematic approach to explore our alternatives alongside human embryonic stem cells in order for the stem cell research community to best serve the citizens of California.